Upper airway dimensions in patients with craniocervical junction malformations with and without sleep apnea. A pilot case-control study

Dimensões da via aérea superior em pacientes com malformações da transição craniocervical com e sem apnéia do sono. Um estudo piloto caso-controle

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The craniocervical transition malformations (CCTM) comprise a spectrum of malformations frequently associated with occipital bone hypoplasia and posterior fossa volume depletion¹,²,3,4,5.

Studies have shown that patients with CCTM tend to suffer more frequently from sleep respiratory disturbances, which are more frequent and severe in patients with basilar invagination. Here we evaluate if patients with CCTM and sleep respiratory disorders (SRD) present smaller airway dimensions than patients without SRD.

Method: Patients with CCTM with and without sleep respiratory disturbances were evaluated clinically by Bindal’s score, modified Mallampati classification, full-night polysomnography and upper airway cone beam tomography.

Results: Eleven patients had sleep respiratory disorders (SRD), and nine patients performed control group without SRD. CCTM patients with SRD were predominantly female, older, had higher BMI, were more likely to have Mallampati grades 3 and 4 and had statistically significant smaller anteroposterior diameter of the upper airway than patients without SRD.

Conclusion: Patients with CCTM and sleep respiratory disturbances have higher BMI, higher Mallampati score and smaller anterior posterior diameter of the upper airway.

Keywords: Chiari type I malformation, sleep apnea, polysomnography.

RESUMO

Objetivo: Pacientes com malformação da transição craniocervical (MTCC) tendem a apresentar mais frequentemente distúrbios respiratórios do sono (DRS), os quais são mais intensos em pacientes com invaginação basilar. O objetivo desse estudo é avaliar se pacientes com MTCC e DRS apresentam dimensões das vias aéreas reduzidas em comparação a pacientes sem DRS.

Método: Pacientes com MTCC com e sem apneia do sono foram avaliados com a escala de Bindal, classificação de Mallampati modificada, polissonografia de noite inteira e tomografia da via aérea superior.

Resultados: Onze pacientes tinham DRS e nove não apresentaram esses distúrbios (grupo controle). Pacientes com MTCC e DRS foram principalmente mulheres, mais velhos, apresentaram maior IMC e maior geadação na escala de Mallampati, além de menor diâmetro anteroposterior de via aérea superior do que pacientes sem DRS.

Conclusão: Pacientes com MTCC e DRS têm maior IMC, maior pontuação na escala de Mallampati e menor diâmetro anteroposterior da via aérea superior.

Palavras-chave: malformação de Chari tipo I, apneia do sono, polissonografia.
We evaluated the possibility that patients with Chiari type I and sleep respiratory disorders (SRD) may present smaller airway dimensions than Chiari type I patients without SRD.

**METHOD**

Patients with signs and symptoms suggestive of Chiari type I malformation and magnetic resonance images compatible with Chiari type I malformation and/or basilar invagination were selected at two Brazilian tertiary hospitals located in Sao Paulo from January to December of 2011. All patients signed a consent form and this clinical study was approved by the Ethics Committee of both institutions.

Signs and symptoms specific for CCTM were evaluated clinically with the scale developed by Bindal et al. Baseline full-night polysomnography (PSG) was performed by trained professionals using the EMBLA system (EMBLA® S7000, Inc., Broomfield, CO, USA). The biological variables were measured with electroencephalography (C3/A2, C4/A1, O1/A2 and O2/A1), electrooculography, submentonian and anterior tibial electromyography and electrocardiography (V2 modified). Airflow was measured through a thermistor and a nasal cannula with a pressure transducer. The thoracic and abdominal movements were monitored with non-calibrated inductance plethysmography; snoring was recorded using a microphone; oxymoglobin was measured with pulse oximetry, and the body position was monitored with a sensor. Sleep scoring was performed by a professional who was trained in polysomnography and was based on the criteria set forth by Rechtschaffen and Kales. The respiratory events and arousals were analyzed according to international criteria.

The patients were divided into two groups based on their PSG results: one with SRD and one without SRD (without central or obstructive sleep apnea). The patients with an apnea/hypopnea index (AHI) greater than or equal to 5 (with a predominance of obstructive events) were considered to have Obstructive Sleep Apnea Syndrome (OSAS) if they presented with at least two of the following signs and symptoms: excessive daily drowsiness, snoring or episodes of respiratory pause observed by others.

The following anthropometric data were evaluated due to their importance in the genesis of SRD: weight, height and body mass index (BMI).

Both groups were evaluated according to the modified Mallampati classification (Figure 1), as proposed by Fredman et al., with the patient seated, the mouth opened maximally and the relaxed tongue inside the oral cavity. The patients were stratified into four groups: (1) grade I: – all of the oropharynx was visible, including the soft palate, the tonsil pillars, the palatine tonsils and the tip of the uvula; (2) grade II: – the soft palate, the faucets and the uvula were visible; (3) grade III: – the soft palate and the uvula base was visible; and (4) grade IV: – the soft palate was not visible et al.10.

The patients classified as Mallampati 1 and 2 and Mallampati 3 and 4 were sub-grouped into two groups for analysis.

All of the patients were subjected to cone beam tomography of the upper airway (Figure 2). The images acquired by the tomography were analyzed in a specialized radiologic center with an I-CAT® (Imaging Sciences International, Hatfield, PA, USA) instrument. All images were calibrated using 36.90 mA, 120 kVp, an exposure time of 40 s, an extended height field of view (FOV) with a volume element of 0.3 mm, and a resolution of 1024 X 1024 pixels and 12 bytes per pixel (4096 gray-scale). For image acquisition, the patient remained seated with eyes open and looking at a mirror in front of him. The patients were positioned using the laser beams of the machine with the Frankfurt plane parallel to the ground and the median sagittal plane perpendicular to the former. Image capture extended from 2 cm above the glabella to the inferior margin of the C4 vertebra. Axial images of 0.3 mm width were obtained and exported in the DICOM (Digital Imaging and Communication in Medicine) format, and then recorded on a CD-ROM.

Dolphin Imaging® 3-D software, version 11.7 (Dolphin Imaging & Solutions, Chatsworth, CA) was used to process the volumetric data (DICOM files) of the nasopharynx (NF), oropharynx (OF), and hypopharynx (HF) to calculate the total volume of these structures and the greatest constriction point.

Figure 1. Mallampati classification.

Figure 2. Upper airway Cone Beam Tomography. The anteroposterior, transverse diameters and cross sectional area at the maximally constricted point of the upper airway in a sleep apnea patient (upper) and in a patient without apnea (lower).
The anteroposterior and transverse diameters were measured and the cross sectional area was calculated during normal respiration and maximal inspiration to delineate the maximally constricted point of the upper airway. The maximum length of the upper airway was measured from the hard palate to the level of the epiglottal tip.

**Statistical analysis**

The anthropometric and image data from both groups were presented as the averages and standard deviations and compared using the Mann-Whitney test. Both genders were compared using the Chi-squared test. The significance level was determined as p < 0.05. The Mallampati data were analyzed among both groups using the Chi-squared test.

**RESULTS**

We studied twenty patients with type I Chiari malformation during the pilot project. Eleven had SRD, and nine did not. Three patients without SRD (WOSRD group, n = 9) were male (33.3%) and 6 were female (66.7%). Among the eleven patients with SRD (WSRD group, n = 11), we studied one man (9.1%) and ten women (90.9%), (Chi-squared p = 0.47). The mean age was 42.28 (± 14) years old in the WOSRD group and 56.15 (± 5.7) years old in the WSRD patients (U 11, p = 0.005). The body mass index (BMI) was 24.21 (± 3.14) among patients in the WOSRD group and 29.24 (± 7.17) in the WSRD patients (U 24.5, p = 0.097) (Table 1).

Concerning the modified Mallampati grade (MMG) among the WOSRD group, three patients had an MMG of 1, three had an MMG of 2, two had an MMG of 3 and one had an MMG of 4. In the WSRD group, none had an MMG of 1, one had an MMG of 2, four had an MMG of 3 and six had an MMG of 4, with a total of 10 patients with an MMG of 3 or 4 in the WSRD group compared with 3 in the WOSRD group (Chi-squared p = 0.003) (Table 2).

**Bindal score**

The mean result for the Bindal clinical score for the WORSRD group was 68.57 (± 41) points compared with 96.92 (± 39) in the WSRD patients (U 29, p = 0.11).

**Polysomnography**

All patients were subjected to polysomnography, and the following data were collected and studied: the exam length, the minutes of sleep, the number of respiratory events, the apnea-hypopnea index (AHI), the number of central, obstructive and mixed apneas, and the lowest, mean and highest oxygen saturation levels (Table 3).

The mean AHI was 3.14 among the WOSRD group compared with 28.75 in the WSRD patients (p = 0.001).

**Computerized tomographic measurements of the pharyngeal airway**

During normal breathing (Figure 3), the WOSRD patients had a pharyngeal anteroposterior diameter of 8.5 ± 1.31 mm compared with 4.73 ± 0.9 mm among the WSRD patients (U 21, p = 0.031). The laterolateral diameter differed between groups (22.6 ± 2.5 vs 18 ± 1.8 mm); however, this difference did not reach statistical significance (U 26.5, p = 0.08). The longitudinal length was 48.78 ± 1.77 mm in the WOSRD patients and 49.46 ± 2.38 mm in the WSRD group (U 49.5, p = 1.0).

In regard to the maximum inspiration, the anteroposterior diameter was 7.29 ± 1.16 mm in the WOSRD patients compared with 5.89 ± 1.47 mm in the WSRD group (U 35.5, p = 0.29), the laterolateral diameter was 19.77 ± 2.72 mm in the first group compared with 17.11 ± 2.52 mm in the second group (U 39, p = 0.45), and the longitudinal length was 49.66 ± 2.41 mm in the WOSRD patients compared with 49.22 ± 2.41 mm in the WSRD group (U 48, p = 0.94).

**DISCUSSION**

Cases of spontaneous respiratory collapse in adult and infant Chiari type I patients have been well documented, resulting in some deaths. During sleep, the voluntary respiratory control becomes attenuated; the maintenance of the respiratory system depends on the automatic ventilatory command, and the patient is more susceptible to respiratory disturbances. This study of sleep respiratory disorders has the potential to reveal SRD in the case of malformations.

With the advent of polysomnography, the respiratory disorders that occur during sleep can be better characterized, and the real importance of CCTM can be better elucidated. Obstructive sleep apnea is the most prevalent respiratory disorder among CCTM patients. Experimental studies have associated CCTM with an abnormality of the occipital somites derived from the paraxial mesoderm. There can be a genetic predisposition to the condition.
Table 3. Polysomnographic data.

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MOF: Minutes of sleep; EL: Exam length; AHI: Apnea-hypopnea index; NCA: Number of central apneas; NOA: Number of obstructive apneas; NMA: Number of mixed apneas; HSaO2: Highest oxygen saturation; MSaO2: Mean oxygen saturation; LSaO2: Lowest oxygen saturation.

*Difference between APNANB and APANB was statistically significant (U 21, p = 0.031). APNANB: Anteroposterior diameter of non-apneic patients during normal breathing; APANB: Anteroposterior diameter of apneic patients during normal breathing; LATNANB: Lateral diameter of non-apneic patients during normal breathing; LATANB: Lateral diameter of apneic patients during normal breathing; LONGNANB: Longitudinal length of non-apneic patients during normal breathing; LONGANB: Longitudinal length of apneic patients during normal breathing.

**Figure 3.** Computerized tomographic measurements of the pharyngeal airway during normal breathing.
Marin-Padilla’s experimental model revealed that, in addition to occipital bone involvement, there is a narrowing of the airway dimensions associated with a posterior fossa volume reduction in these patients.\(^\text{15}\)

Alternatively, Lee RWW et al. have already demonstrated that other factors, such as the growth and development of the maxillomandibular relationships, the maxilla and the mandible relationship to the cranial base, and the growth of local soft and adipose tissues may contribute to upper airway collapse.\(^\text{16}\)

Our main results show that Chiari type I patients with SRD are predominantly female, older, more obese, more likely to have Mallampati grades 3 and 4 and a smaller anteroposterior diameter of the upper airway in comparison with Chiari type I patients without SRD.

Epidemiological studies have shown that the prevalence of OSAS in adults may vary from 1.2% to 7.5%, when considering the presence of EDS and AHI above 5 events per hour of sleep as the diagnostic criteria. A recent epidemiological study, performed in Sao Paulo, that used laboratory polysomnography (the gold standard test for diagnosis of this syndrome), observed that the OSAS prevalence reached the alarming rate of 32% of the analyzed population.\(^\text{17}\) In a study of patients with malformations, the OSAS prevalence reached 68%.

The main risk factors for OSAS are male gender, advanced age and being overweight. Important epidemiological studies have demonstrated that male gender is a well-known risk factor for OSAS, with males being up to four times more affected than females.\(^\text{18}\) The greater tendency of males to exhibit central fat deposition, the protective action of progesterone and the inducing action of testosterone on the collapse of the upper airway and anatomical differences in the airway are some of the possible reasons for this association.\(^\text{19}\) In our sample of Chiari malformation patients WSRD, the frequency of females was greater than for those without WOSRD, even though this was not statistically significant.

Here, we found a higher proportion of older patients among the WSRD group than the WOSRD group, which is consistent with other studies about OSAS. The majority of those studies have strengthened the association between aging and OSAS.\(^\text{17,19,20}\) Tufik et al. revealed that patients older than 84 years of age had a risk of developing OSAS that was 34-fold higher than that of younger patients.\(^\text{17}\) Factors that explain this association include a higher BMI and upper airway compliance, a decreased strength of the esophagus and laryngeal muscles, as well as the lower pulmonary and thyroid function observed in the elderly.\(^\text{21}\)

The main risk factor for OSAS is obesity, and Tufik et al. showed that the risk for OSAS is 10-fold higher in obese patients.\(^\text{17,19,20}\) In addition to the anatomical changes in the upper airway induced by fat accumulation, the respiratory physiology is compromised in obese patients, who have a lower pulmonary volume and compliance, leading to upper airway collapse.\(^\text{22}\)

A Mallampati grade of 3 or 4 has been shown to be an important finding in a physical examination because it has a high positive predictive value for OSAS. This correlation was also true in our sample of CCMT and SRD patients. The difference in the modified Mallampati grade between the groups reached statistical significance, and the patients with SRD had a higher score than those without, consistent with the published data.\(^\text{23,24,25,26}\)

Obesity might be the factor that brings patients with SRD to a higher Mallampati grade. Nashi et al. studied the tongues from 121 consecutive medical examiner cases and observed a high fat content in this organ, mainly in the posterior third. The Nashi group also verified that the weight, volume and fat content of the tongue were associated with a higher BMI, suggesting an association between obesity and a modified Mallampati grade of 3 or 4.\(^\text{27}\) Modern image acquisition studies have shown an association between anatomical characteristics, such as large tongues and narrowed upper airways, and OSAS.\(^\text{28}\)

Shigeta et al. evaluated two groups through computerized tomography, including men and women controlled for age and BMI. The upper airway volume, measured from the dorsal nasal spine to the epiglottal tip, was evaluated. The total height of the oropharynx and the volume of this segment demonstrated a statistically significant difference between genders (larger in men). Among the study participants, the changes increased with age, and age was a significant predictor of the oropharynx length.\(^\text{29,30}\)

The shape and volume of the airway vary in patients with different anteroposterior maxillomandibular relationships. Grauer and colleagues showed that the shape but not the volume of the airway was different according to maxillomandibular vertical relationships.\(^\text{30}\) In the same study, Grauer demonstrated a statistically significant relationship between the inferior portion of the upper airway and the maxillomandibular AP proportion, and between the airway volume and face size and gender. There was no difference between maxillomandibular volume and the vertical proportion. For this purpose, facial CBCT, facial lateral photographs and facial lateral cephalometric radiographs were used.\(^\text{30}\)

Our CBCT findings in CCTM and SRD patients suggest a smaller AP diameter, which corroborates the published data. Adult patients with a Chiari malformation who suffer from sleep apnea have a higher BMI, a higher Mallampati score and a smaller anterior posterior diameter of the upper airway, consistent with the assumption that the dimensions of the airway are a determining factor for sleep apnea in patients with this disease.
References


